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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,808	01/12/2007	Rob Hooft Van Huijsduijnen	294685US0PCT	2174
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OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, L.L.P. 1940 DUKE STREET ALEXANDRIA, VA 22314				
EXAMINER				
WEBB, WALTER E				
ART UNIT		PAPER NUMBER		
1612				
NOTIFICATION DATE		DELIVERY MODE		
12/30/2011		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary**Application No.**

10/590,808

Applicant(s)

HOOFT VAN HUIJSDUIJNEN ET AL.

Examiner

WALTER WEBB

Art Unit

1612

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 September 2011.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) ☒ Claim(s) 1-16, 20 and 21 is/are pending in the application.
- 5a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 6) ☐ Claim(s) ____ is/are allowed.
- 7) ☒ Claim(s) 1-16, 20 and 21 is/are rejected.
- 8) ☐ Claim(s) ____ is/are objected to.
- 9) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 12) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date ____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/15/2011 has been entered.

Applicants' arguments, filed 9/15/2011, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103-previous

Claims 1-16, 20 and 21 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al., (US 2002/0025126) in view of Sowers et al., (Hypertension 2001) and Parissis et al., (International Journal of Cardiology 2002).

Liu et al. teach the compounds instantly claimed. For example, Liu discloses compounds of Formula I, wherein $R_1=CH_2Ph$, R_{2a} and $R_{2b}=H$ and $Cy=phenyl$ substituted with phenyl (see Example 30, at pg. 18). Liu also discloses compounds of Formula I, wherein $R_1=CH_2CH_2Ph$, R_{2a} and $R_{2b}=H$ and $Cy=phenyl$ substituted with -O-

CH₂-quinoline (see Example 11, at pg. 15). Liu also teaches that these compounds are protein tyrosine kinase PTP1B inhibitors useful in treating autoimmune diseases, acute and chronic inflammatory diseases, osteoporosis, obesity, cancer, malignant diseases, and type I and type II diabetes. (See abstract and [0227].)

Liu et al. differs from the instant claims insofar as it does not teach treating coronary obstruction or peripheral vasoconstriction.

Sowers et al. teach that cardiovascular diseases, including atherosclerosis (coronary obstruction), are a major cause of mortality in persons with diabetes. (See abstract and HOPE trial at pg. 1055.) The prior art also teaches that hypertension and endothelial dysfunction are also strongly associated with diabetes patients. (See id.) The prior art goes on to state that each of these diseases serves to exacerbate the other. (See pg. 1053, right col., lines 1-3.)

Sowers et al. do not teach a compound of formula I.

Parissis et al. teach that peripheral vasoconstriction is associated with endothelial dysfunction and hypertension. Patients with hypertension often have a high circulation of endothelin-1, which can result in peripheral vasoconstriction. (See pg. 17, right col. 3rd paragraph to pg. 18, left col. 1st paragraph.). The prior art also teaches that endothelial dysfunction is characterized by a reduction of nitric oxide formation (see pg. 14, left column, lines 19-23).

Parissis et al. do not teach a compound of formula I.

It would have been obvious to a person having ordinary skill in the art at the time of applicant's invention to administer the compounds of Liu for the treatment of

coronary obstruction and peripheral vasoconstriction, since they are problems associated with diabetes. Administering the compounds of Liu to diabetic patients with atherosclerosis and/or hypertension would also treat coronary obstruction and peripheral vasoconstriction. Since endothelial dysfunction is strongly associated with diabetic patients, and hypertensive patients, they would have been expected to have impaired peripheral production of nitric oxide.

Response to Arguments

Applicant argues that impairment of nitric oxide production is not correlated to diabetic conditions (see Remarks at pg. 37).

However, the instant specification states "An endothelial dysfunction, commonly assessed by a decreased endothelial production of NO in response to blood flow, induces an increased peripheral vasoconstriction and therefore an increased peripheral resistance" (see Specification at pg. 2, lines 15-17).

Sowers et al. teaches that endothelial dysfunction is a major risk factor of hypertensive and diabetic patients (see Abstract). Thus, diabetic patients would have been expected to have endothelial dysfunction and, consequently, a decreased production of NO.

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the

application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Walter E. Webb whose telephone number is (571) 270-3287. The examiner can normally be reached on 8:00am-4:00pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Walter E. Webb
/WALTER WEBB/
Primary Examiner, Art Unit 1612